REMARKS

Claims 59-73 have been cancelled. Claims 74-96 are added and are now active and under consideration in this case.

Claims 59-73 stand rejected under 35 USC 112, second paragraph as ostensibly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. See paragraph 5 of the Official Action of May 17, 2006.

Notably, the Examiner has rejected claims 59, 60, 63, 65 and 67 as being ostensibly indefinite for reciting "similarity." The Examiner contends that the definition does not clarify the meaning of this word since the hybridization conditions of high and low stringency are not exemplified. The Examiner contends that the Applicants have not defined the metes and bounds of the "term" substantially similar" and therefore one skilled in the art would not be apprised of the upper and lower limits of activity that are encompassed by substantially "similar biological activities."

All previous claims have been cancelled, and claims 74-91 have been added. With regard to the expression "similarity," the Examiner is referred to the attached Declaration under Rule 1.132 of one of the inventors, Dr. Luc Varin, a person skilled in the art, under who avers that when sequence A is in percent similar to sequence B, it is meant that x % of the positions of an optimal global alignment between sequences A and B consists of conservative substitutions, and that calculating the degree (%) of similarity between two (2) polypeptide sequences, one considers the number of positions at which similarity is observed between corresponding amino acid residues in the two polypeptide

sequences in relation to the entire length of the two molecules being compared. This is well known and understood in the relevant art as Dr. Varin avers.

Furthermore, as demonstrated in the attached Declaration under Rule 1.132, the hybridization conditions are clearly known to person skilled in the art when undertaking such laboratory manipulations. For example, one person skilled in the art may refer to a textbook in the art such as chapter 9 of the book Molecular Cloning: A Laboratory Manual from Sambrook, Fritsch and Maniatis (ISBN: 087969-309-s6, Cold Spring Harbor Laboratory Publisher). Applicants, thus submit that reciting the hybridization condition would be unnecessary as this information would be considered routine by those skilled in the art. It is also well-established that Applicants need not describe in their specification what is already well-known in the art. In fact, it is preferred that Applicants omit what is known in the art. *Hybritech, Inc.* v. *Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987).

With regard to "functional homologue" and "similar biological activities," Applicants also submit that it is clear from the definition of functional homologue appearing on pages 8 and 9 that by substantially similar biological activity it is meant an 11- or 12 hydroxyjasmonic sulfotransferase activity. In this regard, the Examiner is referred to the diagram appearing on page 13 of the specification where it is clear that the enzyme affecting flowering time is the enzyme that catalyzes 11-hydroxy jasmonate or 12-hydroxyjasmonate into 11- or 12- hydroxy jasmonate sulfate. Hence, Applicants submit that the metes and bounds of "substantially similar" can very well be appraised by a persons skilled in the art. Applicants, thus, respectfully submit that the expressions "similarity" and "functional homologue" are clear to a person skilled in the art and hence,

well defined, thus satisfying 35 USC 112, first paragraph. Hence, this ground of rejection is deemed moot.

Claims 70-72 stand rejected under 35 USC 112 first paragraph as ostensibly failing to comply with the written description requirement. See paragraph 6. In this regard, the Examiner is referred to page 6, lines 1 and 2 of the specification wherein it is clear that the present invention is directed to induce flowering in horticultural plants of economic importance and in crop plants such as cauliflower and broccoli thus providing proper support for such claims. Furthermore, as demonstrated in the Declaration under Rule 1.132 the specification does convey to one skilled in the art that the inventors had possession of the invention at the time the present application was filed. Hence, this ground of rejection is deemed moot.

Claims 59-73 stand rejected under 35 USC 112 first paragraph as ostensibly containing subject matter which would not be described in the specification in such as way as to reasonably convey one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. See paragraph 7. The Examiner has added that because of the indefiniteness of "similarity" and "functional homologue," the recitation "similarity" and "functional homologue" carries no weight and, moreover, the Office has broadly interpreted the claims to encompass any nucleic acid sequence encoding any protein having biological activity or any amino acid sequence having biological activity. Furthermore, the Examiner has rejected the expression "functional homologue" and has alleged that the Applicants have not explicitly defined a "substantially similar biological activity" as 11-/12-

hydroxyjasmonate sulfotransferase and therefore, the Examiner contends that the reaction "functional homologue" carries no weight.

Applicants respectfully traverse this rejection and submit that they have demonstrated above that the expression "similarity" is clear to a person skilled in the art and hence, is definite. Thus, for such a person, it would be clear that the claims do not read on any nucleic acid sequence encoding any protein, having biological activity or any amino acid sequence having biological activity. It is clear for such a person skilled in the art that the claims read on SEQ ID. NO:3 and functional homologues of SEQ ID NO:3. The Applicants have also demonstrated above that a functional homologue is a protein having a similar biological activity as SEQ ID NO:3, i.e., a sulfotransferase activity.

Furthermore, the Examiner has contended that Applicants do not identify essential regions of the protein encoded by SEQ ID NO:1, nor do they disclose any polynucleotides encoding any polypeptides that are functional homologues of any sulfotransferase that can be used to alter the level of any compound listed above listed in claim 59. The Examiner has further cited *University of California* v. *Eli Lilly and Co.*, 43 USPQ 2d 1398 (Fed. Cir. 1997), page 6 lines 3 and 4. Applicants submit that the sequence described in the present application contains the motifs that are well-known to be present in all soluble sulfotransferases that have been characterized. This information is readily available by conducting a protein blast search at NCBI.[1] Indeed, Applicants have demonstrated in the Declaration under Rule 1.132 that it is very easy for one person skilled in the art to find these conserved domains and to assess the sulfotransferase

[1] See the attached description of "BLAST" from wikipedia.org.

function to an unknown protein having these motifs and by having these conserved domains to identify in databases protein sequences having sulfotransferase activity.

The Examiner is further referred to example 1 of the annexed Declaration under Rule 1.132 where it is clearly shown that such an approach is facile for one skilled in the art. In that example, it is demonstrated that a person skilled in the art of molecular biology could easily use the information disclosed in the present specification to retrieve other sulfotransferase coding genes having the same function as AtST2a [12 hydroxyjamonate sulfotransferase (SEQ ID NO:3)]. Hence, in this particular case, it is not necessary to disclose in the present specification all sequences having a sulfotransferase activity or coding for a sulfotransferase as this information is readily available to those skilled in the art. It is not necessary to disclose a representative number of plant species encoding a sulfotransferase altering the level of any compound listed in claim 59 nor is it necessary to describe structural features common to members of the claimed genus of polynucleotides as this information need not be disclosed in the present specification in order to practice the present invention as claimed.

Finally, the Examiner has contended that Applicants have failed to describe structural features common to members of the claimed genus of polynucleotides. Applicants traverse this comment and submit that such a description is unnecessary since genetic databases as of the filing date of this application have listed several sequences for sulfotranferases. The Examiner is once more referred to the annexed Declaration under Rule 1.132, where the cladogram shows that the sulfotransferase enzyme is highly conserved among plant species and where it is demonstrated that by using the

information found in the specification one person skilled in the art could easily practice the present invention as claimed. Hence, this ground of rejection is deemed moot.

Claims 59-73 stand rejected under 35 USC, first paragraph ostensibly because the specification while being enabling for a method of increasing the time to flowering in *Arabiposis* plants entailing transforming said plants with *Arabidopsis* AtST2a genomic sequence of SEQ ID NO:1, operably linked to a promoter in antisense orientation, wherein the levels of 11- or 12- hydroxyjasmonic acid are increased relative to non-transgenic plants, does not reasonably provide enablement for any method that accelerates flowering in a plant comprising modifying the endogenous level of at least one of any of claimed compounds listed in claim 59, or a method for producing a transgenic plant which flowers early entailing expressing a sulfotransferase encoded by SEQ ID NO:1 or a functional homologue having at least 80% similarity to SEQ ID NO:1, or containing a sequencing that is antisense to a nucleic acid of SEQ ID NO:1 or antisense to a nucleic acid sequence which is a functional homologue having at least 80% similarity to SEQ ID NO:1. See paragraph 8. The specification is said to not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The Examiner has also rejected the claims in view of *In re Wands*, USPQ 2d 12400 (Fed. Cir. 1988), which lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. Furthermore, the Examiner has again brought up the ostensible indefiniteness of the recitation of "similarity" and "functional homologue." The Examiner referring to Harms et al. (12995, The Plant Cell, 7:1645-1654) has also contended that the state of the

art teaches that transforming a plant with a nucleic acid molecule encoding a protein involved in jasmonic acid biochemistry does not lead to predictable results.

Applicants respectfully traverse all aspects of this rejection and refer to examples 2 and 3 on pages 28 and 29 of the specification where it is clearly shown that the Applicants were in possession of *Arabidopsis* plants exhibiting late flowering and *Arabidopsis* plants exhibiting early flowering as compared to a non-transformed plant.

Furthermore, Applicants submit that from the annexed Rule 1.132 Declaration, it is clear that in view of the amount of direction or guidance presented in the application, the working example present in the application would provide adequate guidance to one skilled in the art to easily arrive to the invention as claimed without undue experimentation. Furthermore, it has also been demonstrated in the annexed Rule 1.132 Declaration that in view of the nature of the present invention, it is well-known by one skilled in the art of transforming plants, that after a transformation, reasonable selection of the plants is required. In this case, the selection is easy and relies upon a plant characteristic observed with the naked eye i.e. appearance of the first flower. Such a selection methodology is clearly within the routine skill of the artisan. Hence, this rejection is deemed moot.

The Examiner refers to the work by Harms et al. published in Plant Cell to support his conclusion that transforming a plant with a nucleic acid encoding an enzyme involved in jasmonic acid (JA) biosynthesis does not lead to predictable results. However, to be sure, Applicants submit that Harms et al. demonstrates that, as expected, the overexpression of AOS did lead to a significant increase in JA. It is well known that the constitutive expression of genes involved in the wounding response leads to plants

that grow poorly. The transgenic overaccumulating JA responded by decreasing their sensitivity to JA. This feedback mechanism is not observed when there is an overaccumulation of 12-hydroxyjasmonate in transgenic *A. thaliana*. The difference in the response is most likely linked to the nature of the two compounds. It is also known that treatments of plants with JA induce an arrest of growth that is not observed following 12-hydroxyjasmonate treatments. As also shown in the present specification, treatment with 12-hydroxyjasmonate was shown to induce precocious flowering and no side effects. It was observed that the overaccumulation of 12-hydroxyjasmonate caused transgenic plants to flower earlier. Furthermore, as demonstrated in the annexed Declaration under Rule 1.132, the results obtained with *Brassica napus* demonstrate that the effect on flowering time is not restricted to *A. thaliana*. Applicants also submit that jasmonic acid and 12-hydroxy jasmonate have different effects on gene expression. In this regard, the Examiner is referred to the annexed results (See Annex A) that illustrate the difference between the effects mediated by jasmonic acid and 12-hydroxy jasmonate and gene expression from an mRNA profiling experiment performed with the *Arabidopsis taliana* Affymetrix DNA chips. Hence, this rejection is deemed moot.

On page 9 of the Office Action, the Examiner has also contended that the state of the art is such that one of ordinary skill in the art cannot predict which nucleic acids that are at least 80% similar to SEQ ID NO:1 will encode a protein with the same activity as a protein encoded by SEQ ID NO:1. Applicants submit that it has been demonstrated in the annexed Declaration under Rule 1.132 that one skilled in the art of molecular biology could easily use the information described in the present specification to retrieve other sulfotransferase coding genes having the same biochemical functions as AtST2A. Hence,

it is clear that the state of the art is such that one of skill in the art could easily predict which nucleic acids that are at least 60% homologous to SEQ ID NO:1 would encode a protein with the same activity as a protein encoded by SEQ ID NO:1. The state of the art is also such that one of skill in the art can predict which protein at least 60% homologous to SEQ ID NO:3 will have the same activity.

The Examiner has referred to Bowie et al. (Sciences, 247:1306-1310, 1990) opining that predicting protein structure from its sequence data and, in turn utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex. In this regard, Applicants submit that sequence comparison coupled with phylogenetic analysis allows restricting the number of sequences that one has to clone to find an operable sequence. It is demonstrated in Example 1 and 2 of the annexed Declaration under Rule 1.132 that the hybridization approach as well as the sequence comparison approach both allow one skilled in the art to select enzymes from complex genomes. One skilled in the art would easily apply these commonly used approaches to isolate a functional homologue of the *A. thaliana* 12-hydroxyjasmonate sulfotransferase. Another commonly used approach would be to clone all sulfotransferase-coding genes from one species (15-20 cDNA sequences) in bacterial expression vectors and assay the recombinant proteins with the appropriate substrate. This well-known approach can also allow for the identification of the sequence coding for the proper enzyme. As the Examiner may surely understand, the important thing to remember is that such an enzyme exists in the genome and that several different known approaches are available to one skilled in the art in order to identify the gene encoding it.

The Examiner has further noted, as an example of the apparent unpredictability of plant transformation, the example of replacing of a glycine residue located within the start domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, thereby altering the sterol/lipid binding domain as disclosed by McConnell *et al.* (Nature, 411 (8838): 709-713, 2001). Although this may be true in the case of sterol/lipid binding domain, Applicants have demonstrated in the annexed Declaration that the state of the art of sulfotransferases makes it feasible to predict the function of a sulfotransferase by comparing its sequence to AtST2A. Thus, the metes and bounds of protein sequences having the same function as AtST2A are well-defined. Applicants have also shown in the annexed Declaration that the conserved and variable regions of sulfotransferases were retrievable from genetic and protein public databases at the time of filing. Thus, it is unwarranted to draw conclusions about the present invention (with sulfotransferases) from a reference related to sterol/lipid binding domains.

In view of the above, Applicants assert that the citations by Bowie *et al.* and McConnell *et al.* are not relevant to the present invention.

On page 10 of the Office Action, the Examiner has contended that the state of the art teaches that antisense technology produces unpredictable results (Bryant, 1989, Trends in Biotechnology, 7(2): 20-21) and that using sequences that are not 100% identical to the target sequence will not produce expected results (Emery *et al.* 2003, Current Biology, 13: 1768-1774). Applicants respectfully traverse this position and submit that Bryant shows that a wide array of phenotypes from plants exhibiting suppression to plants exhibiting wild type levels of CHS were obtained in an antisense

transformation experiment. Bryant suggested that the position of insertion of the transgene was affecting its level of expression. This is one of several examples where this phenomenon has been observed. Plant molecular biologists devising a plant transformation experiment would be well aware of this fact. This is why it is important to select a number of transgenic lines to allow finding ones expressing the transgene at an adequate level. Typically, more than 100 independent events are screened for each construct to find the right ones. As a person of skill in the art would appreciate, the effect of the position of the transgene on the level of expression does not preclude the isolation of the proper transgenic lines expressing the proper phenotype. In the case of the present application one selects the plants wherein flowering time has been modified. This is easily done since it is possible to observe this phenotype by the naked eye. Hence, one skilled in the art would be able to select the best plant or group of plants after antisense transformation.

In the second paragraph of page 10, the Examiner has contented that Applicants have not disclosed how one makes or isolates any of the sequences that are encompassed by Applicants' claims. In this regard, Applicants submit that in the absence of any other information, one skilled in the art would use the sequence published in the present specification to generate a probe to screen other genomes for the presence of homologous sequences. One skilled in the art would know which region of the respective polynucleotides could be used to amplify any of the polynucleotides or which region could be used as a probe to isolate any of the polynucleotide sequences. This is exactly the approach that was used to isolate BnST2 in the first example of the annexed Declaration under Rule 1.132. Hence, this methodology works quite well. Furthermore,

at the time of filing the present application, the conserved domains present in all sulfotransferases were already documented. (See Varin et al. Proc Natl Acad Sci U S A. 1992 Feb 15; 89(4):1286-90). Based on this information, oligonucleotides could be easily deduced from the conserved sequences, for PCR amplification. However, the simplest way would be to screen a cDNA library with the sequence published in the present application. Once identified, the sequence could be expressed in *E. coli* and tested for 12-OHJA activity. As the Examiner must surely agree, one skilled in the art would have been able to apply without difficulty these methodologies at the time the present application was filed as they are both well-known and routine to those skilled in the art.

At the bottom of page 10, the Examiner has rejected claim 59 for reciting "modifying" and "alter". In response to this rejection, new claims are provided which do not use these terms.

On page 11, the Examiner has rejected claim 64 because it recites applying to a plant one of the compounds listed in claim 64. In this regard, the Examiner is respectfully referred to the examples section B results at the bottom of page 27 and top of page 28 of the specification where it is shown that it is possible to induce flower formation by the exogenous application of 12-hydroxyjasmonate and/or other compounds of the jasmonate family to crop plants.

The Examiner has also rejected claim 66 because Applicants have ostensibly not disclosed examples on how to increase the endogenous level of hydroxylase which hydroxylates jasmonic acid or methyljasmonic acid. This claim has been deleted hence this rejection has been rendered moot.

In the 3rd paragraph of page 11 of the Office Action, the Examiner has contended that in the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences. Applicants respectfully disagree with the Examiner and submit that new isolated sequences must be tested in-vitro before using them for the production of transgenic plants. However, plant genomes contain only a limited number of different sulfotransferases and it would be very easy to assay all of them. Finally, there are several tools to restrict the choice of the proper sequences such as sequence comparison and phylogenetic trees (as demonstrated in the annexed Declaration under Rule 1.132).
It is clear from Wands that even the necessity of excessive screening procedures (to isolate a claimed cell) is not "undue experimentation" where the required screening methods are routine in the art. The facts under consideration in the present case are even more conservative than the facts in Wands and, thus, even more solidly in accord with 35 USC 112, as pertains to the law of enablement and undue experimentation.

Specifically, there are only a limited number of plant sulfotransferases, and all could be readily identified and assayed using known (or routine) methodologies. Further, even this facile process may be rendered even easier by first restricting the choice of sulfotransferase sequences for assaying by sequence comparison and using phylogenetic tress, all of which use known and readily available information to those skilled in the art.

However, and perhaps of greater importance is the fact that the annexed Rule 132 Declaration demonstrates the effectiveness of decreasing the expression of a sulfotransferase having at least 60% homology to SEQ ID No:3. See, in particular, the comments in the "Summary" and Annex 1 in the Declaration. The Declaration also

clearly evidences the effectiveness of decreasing the expression of a sulfotransferase having at least 80% homology to SEQ ID No:3.

Hence, this ground of rejection is deemed moot.

In paragraph 9, the Examiner has rejected claims 59 - 61 under 35 USC 102(b) as being anticipated by Weigel (U.S. Patent No. 5,844,119) because of the indefiniteness of "similarity" and "functional homologue". Applicants respectfully traverse this rejection and submit that in view of the argument submitted concerning the expressions "similarity" and "functional homologue", it is now clear that these words are definite and that the breadth of the claim is also defined.

On the other hand, Weigel et al. discloses a transgenic plant that has accelerated flower meristem development and methods to produce the plant. However, Weigel et al. does not disclose a plant or a method to produce such plant with an accelerated flowering time by increasing the level of 11- or 12-hydroxy jasmonate in the plant or decreasing the level of at least one compound of sulfate ester of 12-hydroxyjasmonic acid and sulfate ester of 11-hydroxyjasmonic acid. Hence, it is clear that the present invention is neither disclosed nor suggested by Weigel et al. Hence, this ground of rejection is deemed unsustainable and should be withdrawn.

All of the above amendments are fully supported by the claims and disclosure as originally filed. No new matter has been added.

In view of all of the above, it is believed that this application is now in condition for allowance.

To the extend necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of

this paper, including extension of time fees, to Deposit Account 13-2725 and please credit any excess fees to such Deposit Account.

CONCLUSION

In view of the above amendments, remarks, and attached Rule 132 Declaration, it is believed that the present application is now in condition for allowance. Early notice to this effect is earnestly solicited. Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

MERCHANT & GOULD P.C.

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